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Original article

Incretin effects, gastric emptying and insulin responses to low oral glucose loads in patients after gastric bypass and lean and obese controls

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Abstract

Background: After laparoscopic Roux-en-Y gastric bypass (LRYGB), many patients suffer from dumping syndrome. Oral glucose tolerance tests are usually carried out with 50–75 g of glucose. The aim of this study was to examine whether minimal glucose loads of 10 g and 25 g induce a reliable secretion of satiation peptides without dumping symptoms after LRYGB. In addition, lean and obese controls were examined.

Objective: The objective of this study was to determine the effects of low oral glucose loads on incretin release and gastric emptying.

Setting: All surgical procedures were performed by the same surgeon (RP) at the St. Claraspital Basel in Switzerland. Oral glucose challenges were carried out at the University Hospital of Basel (Phase 1 Research Unit).

Methods: Eight patients 10 ± .4 weeks after LRYGB (PostOP; body mass index [BMI]: 38.6 kg/m^2 ± 1.7) as well as 12 lean controls (LC; BMI: 21.8 kg/m^2 ± .6) and 12 obese controls (OC; BMI 38.7 kg/m^2 ± 1.3) received 10 g and 25 g of oral glucose. We examined clinical signs of dumping syndrome; plasma glucose, insulin, glucagon-like peptide 1, glucose-dependent insulinotropic peptide, and peptide tyrosine tyrosine concentrations; and gastric emptying with a ^{13}C-sodium acetate breath test.

Results: No signs of dumping were seen in PostOP. Compared with OC, LC showed lower fasting glucose, insulin, and C-peptide, and lower homeostasis model assessment (HOMA) and AUC-180 for insulin and C-peptide. In PostOP, fasting insulin, HOMA and AUC-180 for insulin was lower and no difference was found in fasting C-peptide or AUC-180 for C-peptide compared to OC. There was no significant difference in fasting glucose, insulin, C-peptide, HOMA and AUC-180 for insulin in PostOP compared to LC, but AUC-180 for C-peptide was higher in PostOP. AUC-60 for gut hormones was similar in OC and LC and higher in PostOP compared to OC or LC. gastric emptying was slower in LC and OC compared with PostOP.

Conclusion: After LRYGB, 25 g oral glucose is well tolerated and leads to reliable secretion of gut hormones. Fasting glucose, insulin and C-peptide are normalized, while glucagon-like peptide 1, glucose-dependent insulinotropic peptide and peptide tyrosine tyrosine are overcorrected. Pouch emptying is accelerated after LRYGB. (Surg Obes Relat Dis 2016;12:1320–1328.) © 2016 American Society for Metabolic and Bariatric Surgery. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Keywords: Obesity; Bariatric surgery; Oral glucose tolerance test; Gastric emptying; Incretins

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After Roux-en-Y gastric bypass (RYGB), many patients suffer from early and/or late dumping syndrome as a reaction to carbohydrate-rich meals. *Early dumping* is

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caused by faster nutrition release to the intestine, which leads to osmotically-driven fluid shifts from the blood to the lumen and, thus, vasomotor symptoms. The marked increased secretion of gastrointestinal hormones, such as glucagon-like peptide 1 (GLP-1), after RYGB probably contributes to early dumping [1]. *Late dumping* occurs 1–3 hours after eating and is caused by hyperinsulinemia and is therefore characterized by symptoms of hypoglycemia-like weakness, sweating, and dizziness. But how much glucose is too much? A clear threshold above which symptoms of dumping syndrome are to be expected is missing in the literature. Oral glucose tolerance tests in non-operated patients are usually carried out with 75 g of glucose. For stimulation of incretin release with glucose, glucose loads of 50–75 g are most commonly used. From practical experience, we know that patients after gastric bypass do not always tolerate glucose loads commonly used in an oral glucose tolerance test (OGTT). To study incretin and gut hormone release—for example, GLP-1—a minimal delivery of 2 kcal/min solution into the intestine is needed. However, as gastric emptying (or rather pouch emptying) is accelerated after RYGB, we hypothesized that less glucose is necessary to reach this threshold of 2 kcal/min.

The aim of this study was therefore to examine whether minimal glucose loads of 10 g and 25 g induce a reliable secretion of incretin and satiation peptides without dumping symptoms in patients after gastric bypass.

Materials and Methods

The protocol was approved by the Ethics Committee of Basel, Switzerland (EKBB: 272/05) and conducted in accordance with the principles of the Declaration of Helsinki. All patients gave written informed consent. The trial is registered in the clinical trials registry of the National Institutes of Health (NCT01851616) and was funded by the Swiss National Science Foundation (grant no. 138 157).

Between December 2012 and February 2013, 8 morbidly obese, female patients (mean body mass index [BMI]: 38.6 ± 1.7 kg/m^2, range = 32.5–46.9 kg/m^2; mean age: 35.8 ± 1.7 years, range = 23–47 years) were recruited 10 ± .4 weeks after laparoscopic bypass surgery. Exclusion criteria were: age >50 years, diabetes, smoking, substance abuse, regular intake of prokinetic drugs and a history of gastrointestinal surgery other than laparoscopic Roux-en-Y gastric bypass (LRYGB). Mean excessive BMI lost at the first visit in relation to preoperative BMI was 25.9 ± 3.6% (range = 19.0–24.6%).

Twelve lean, healthy volunteers (mean BMI: 21.8 ± .6 kg/m^2, range = 19.0–24.6 kg/m^2; 6 female and 6 male, mean age: 24.7 ± .9 years, range = 20–32 years) and 12 obese volunteers (mean BMI: 38.7 ± 1.3 kg/m^2, range = 30.5–47.8 kg/m^2; 6 female and 6 male, mean age: 28.8 years ± 2.6, range = 19–47) were recruited by word of mouth. Exclusion criteria were the same as in postoperative patients. In addition, BMI between 18 and 25 kg/m^2, respectively >30 kg/m^2, was required.

All patients were seen on 2 occasions, with an interval of 1–2 weeks. After an overnight fast, patients were admitted to our Phase 1 Research Unit at 8.30 h. Baseline heart rate and blood pressure were measured and a peripheral venous catheter was placed. After taking fasting breath and blood samples, each subject received a cup with 10 g or 25 g of glucose in 200 mL tap water and 50 mg ^{13}C-sodium acetate (for determination of gastric emptying rates). The treatment order was randomized within a subject. Patients were asked to drink the solution within 5 minutes. Throughout the test, patients remained in a sitting position in a comfortable chair. Breath samples for determination of gastric emptying rate were collected in foil bags at –1, 15, 30, 45, 60, 75, 90, 105, 120, 150, 180, 210 and 240 minutes. Blood samples for measurement of plasma glucose, insulin, GLP-1, and glucose-dependent insulinotropic peptide (GIP) were taken at –10, –1, 15, 30, 45, 60, 90, 120 and 180 minutes.

In all patients, gastric emptying rates were assessed using the ^{13}C-sodium acetate breath test. This test is an accurate, noninvasive, simple method without radiation exposure and represents a reliable alternative to scintigraphy, the gold standard for measuring gastric emptying [2,3]. The test solution is labeled with 50 mg ^{13}C-sodium acetate; the substrate is rapidly absorbed in the proximal small intestine, metabolized in the liver with the production of $^{13}CO_2$, which is exhaled rapidly, thus, reflecting gastric emptying of nutrients in patients with intact anatomy of the gastrointestinal tract [2,3]. Patients were asked to exhale through a mouthpiece to collect an end-expiratory breath sample into a 100 mL foil bag at certain time intervals. The $^{13}CO_2$ breath content was determined by nondispersive infrared spectroscopy using an isotope ratio mass spectrophotometer (Wagner Analysen Technik, Bremen, Germany). ^{13}C-abundance in breath is expressed as relative difference (δ ‰) from the universal reference standard (carbon from Pee Dee Belemnite limestone). ^{13}C-enrichment is defined as the difference between preprandial ^{13}C-abundance in breath and ^{13}C-abundance at the defined postprandial time points and is given in δ over basal.

Delta values were converted into atom percent excess and then into percent of administered dose of ^{13}C excreted per hour (%dose/h (%)). In this last conversion, the CO_2 production of the subjects was used, which is assumed to be 300 mmol/h multiplied by the body surface area. The body surface area was calculated by the weight-height formula of Haycock et al [4]. Whole blood and plasma glucose concentrations were measured by a commercially-available glucose oxidase method (Bayer Consumer Care AG, Basel, Switzerland). The lowest level of glucose that can be detected by this assay is .6 mmol/L. Insulin was measured with a commercially-available enzyme-linked immunosorbent assay kit (Abnova, Taipei City). The intra- and interassay coefficients of variation are below 8.1% and 8.5%. Gut

hormones were measured by an Immunological Multi-Parameter Chip Technology (Roche Diagnostics GmbH, Penzberg, Germany). The intra- and interassay coefficients of variation are below 9.5% and 10.0%, respectively.

In patients after LRYGB, signs of dumping were evaluated in addition to the above-mentioned examinations: Whole blood glucose was directly measured by means of an Accu-chek (Roche Diabetes Care, Rotkreuz, Switzerland) device at 0, 15, 30, 45, 60, 90, 120, 180, and 240 minutes. Hypoglycemia of $\leq$3.5 mmol/L would have been followed by immediate study termination for the patient and i.v.-glucose infusion. In addition, clinical signs of dumping were recorded and a dumping score applied. Clinical signs were defined as follows: Oral glucose stimulation test was considered positive for early dumping if at 30 minutes an increase in heart rate $>$10 beats/min from baseline or an increase in hematocrit $>$10% from baseline was found. The test was considered positive for late dumping if at 180 minutes late hypoglycemia occurred (glycaemia $<$3.5 g/dL) [5].

A dumping severity score developed by Arts et al. was applied: After glucose intake, the patient was asked to grade the intensity (scale, 0–3; 0, absent; 1, mild; 2, relevant; and 3, severe, interfering with daily activities) of 8 early dumping symptoms (sweating, flushing, dizziness, palpitations, abdominal pain, diarrhea, bloating, and nausea) and 6 late dumping symptoms (sweating, palpitations, hunger, drowsiness/unconsciousness, tremor, and irritability). A questionnaire for grading early symptoms was filled in by the patient 30 minutes and 1 hour after glucose intake and for late symptoms after 90, 120, 180, and 240 minutes. An early and late dumping severity score was calculated by adding the severities of all early and late dumping symptoms. The mean of the 2 early time points was used as an "early dumping score" (maximum: 24 points), and the mean of the 4 late time points was taken as a "late dumping score" (maximum 18 points). A cumulative dumping severity score was obtained by adding early and late scores [5].

Descriptive statistics were used for demographic variables, such as age, weight, height, and BMI. Data of plasma hormones were evaluated by area and plasma concentration time curves (AUC) and maximum plasma concentrations (Cmax). Based on published results, it was anticipated that AUC-60 would be sufficient for incretin release. For insulin and glucose analysis, AUC-180 was calculated, as dynamics are different from incretins and late dumping occurs after 60 minutes. Dose-response, with regard to increasing glucose loads within the groups, was analyzed by *t* test. For differences between the 3 groups, univariate analysis of variance with Bonferroni correction was used.

The purpose of this study is to gain basic information on the physiologic role of the aforementioned low doses of glucose on incretin release and gastric emptying. The sample size of this study was chosen on the basis of practical considerations rather than statistical estimation. However, according to our experience, a sample size of 8–12 patients will most likely allow us to detect large differences in parameters ($>$50%) between the treatments groups. For all statistical analysis, we used SPSS for Windows software (version 21.0). Differences were considered as significant when $P \leq .05$.

Materials

Glucosum anhydricum was purchased at Hänseler AG, Herisau, Switzerland, and ^{13}C-sodium acetate was purchased at ReseaChem GmbH, Burgdorf, Switzerland.

Results

Complete data from 8 postoperative patients, 12 lean controls (LC), and 12 obese controls (OC) were obtained for analysis. No adverse events were reported.

Dumping syndrome

There were no clinical signs of dumping in patients after LRYGB. At 30 minutes, no increase in heart rate $>$10 beats/min from baseline was found nor did we find any changes in hematocrit. None of the patients had to terminate the study due to hypoglycemia $\leq$3.5 mmol/L. Dumping scores for early and late signs of dumping according to Arts

Table 1
Fasting values in morbidly obese patients 6–8 weeks after laparoscopic Roux-ex-Y gastric bypass versus lean and obese controls

Parameter	Lean controls	Obese controls	PostOP patients	*P*-Value		
	|a)|			a)	b)	c)
	|b)|					
	|c)|					
Fasting insulin (μU/mL)	4.4 ± .5	16.7 ± 2.1	6.2 ± 1.1	**<.001**	1.0	**<.001**
Fasting glucose (mmol/L)	4.9 ± .1	5.2 ± .1	4.9 ± .1	.07	1.0	**.03**
Fasting C-peptide (ng/mL)	3.7 ± .3	6.1 ± .4	5.4 ± .8	1.0	.08	**.003**
Homeostasis model assessment	1.0 ± .1	3.8 ± .5	1.4 ± .3	**<.001**	1.0	**<.001**
Insulin/C-peptide molar ratio	.02 ± .001	.05 ± .005	.02 ± .002	**<.001**	1.0	**<.001**

Data are expressed as mean ± standard error of the mean. N = 8 PostOP, 12 obese controls, and 12 lean controls.
P values: a) Obese versus PostOP, b) Lean versus PostOP, c) Lean versus Obese; (bold $<$.05)

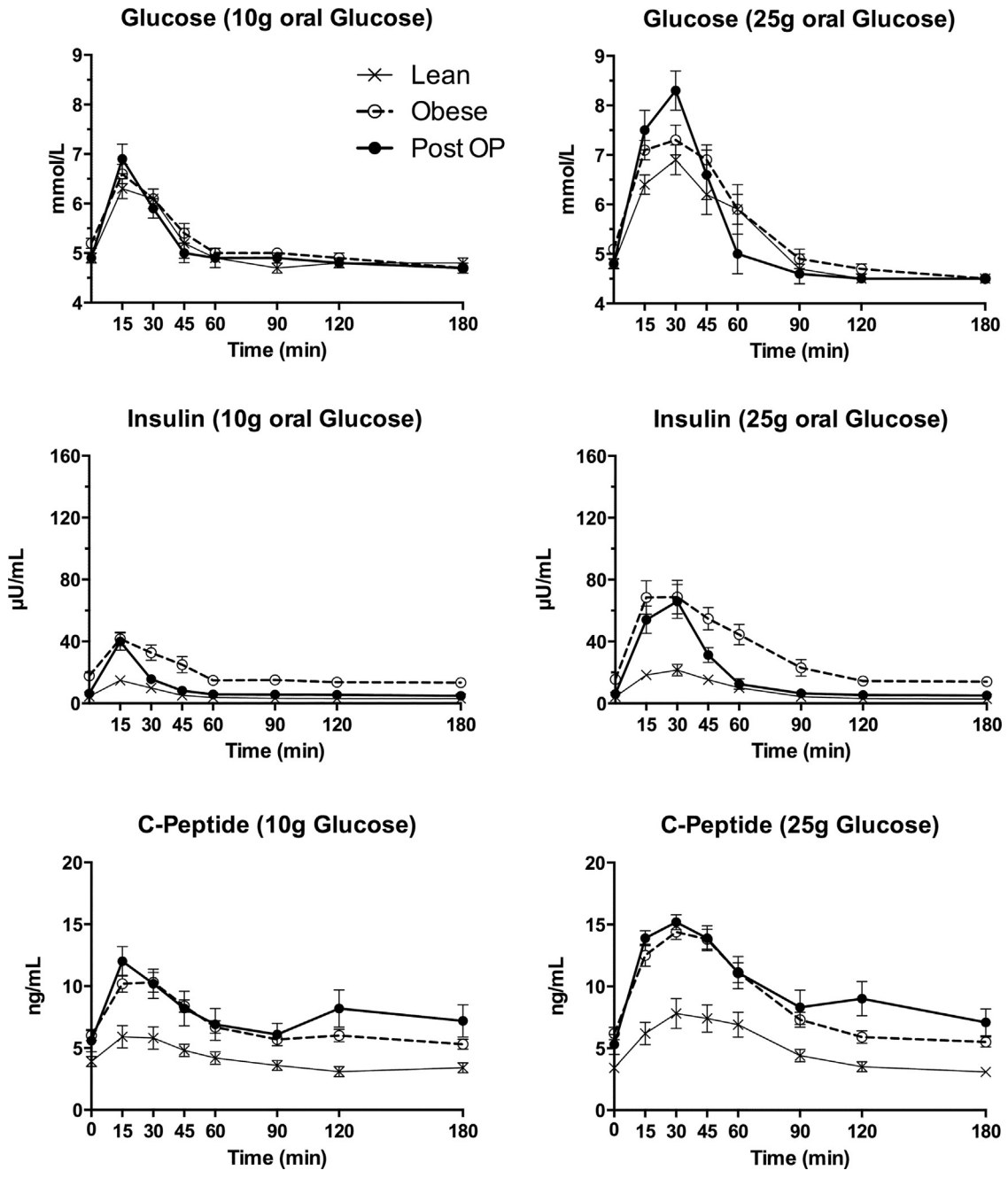

Fig. 1. Insulin, plasma glucose and C-peptide after 10 g and 25 g glucose ingestion. Data are expressed as mean ± standard error of the mean. N = 8 PostOP (10 ± .4 weeks after laparoscopic Roux-en-Y gastric bypass) patients, 12 obese controls, and 12 lean controls.

et al. were negative in all postoperative patients as well: of the 8 early dumping symptoms, 2 patients had slight to moderate dizziness (severity score 1–2) after 10 g of glucose, 2 patients experienced slight nausea (severity score 1), and 1 experienced slight dizziness (severity score 1) after 25 g of glucose. The patients reached a total mean score for signs of early dumping of .4 ± .2 (range = 0–2) out of a maximum of 24 points after 10 g of glucose and a score of .2 ± .1 (range = 0–1) after 25 g of glucose. Of the 6 late dumping symptoms (sweating, palpitations, hunger, drowsiness/unconsciousness, tremor, and irritability), all 8 patients were hungry (severity score 1–3) and 7 described drowsiness (severity score 1–2); no other symptoms were mentioned. Patients reached a total mean score for signs of late dumping of 2.0 ± .3 (range = 0–4) after 10 g of glucose and a score of 1.1 ± .3 (range = 0–5) after 25 g of glucose out of a maximum of 18 points. The cumulative dumping severity score was obtained by adding early and late scores: 2.3 ± .4 after 10 g of glucose and 1.3 ± .3 after 25 g of glucose out of a maximum of 42 points.

Lean versus obese controls

LC showed significant lower fasting glucose and insulin values than OC and as a consequence homeostasis model assessment (HOMA) index (HOMA = fasting insulin μU/mL × fasting glucose mmol/L / 22.5) was also much lower. The AUC-180 for insulin was significantly lower after 10 g and 25 g of oral glucose in LC compared to OC. Fasting C-peptide was significantly lower in LC, and AUC-180 for C-peptide was significantly lower after both glucose loads in LC compared with OC (Table 1, Fig. 1). In contrast, AUC-60 for active glucagon-like peptide 1 (aGLP-1), total glucose-dependent insulinotropic peptide (tGIP), and peptide tyrosine tyrosine (PYY) were not significantly different between LC and OC (Table 2, Fig. 2). Molar insulin/C-peptide ratio was significantly lower in lean versus obese patients (Table 1).

Obese versus PostOP

After LRYGB, fasting glucose was not significantly lower, in contrast to fasting insulin and HOMA, for which statistically significant lower values were observed. AUC-180 for insulin was significantly lower in postoperative patients after 25 g of oral glucose but not after 10 g of glucose. There was no statistically significant difference between the 2 groups for incremental AUC-180 after either glucose load. After both 10 g and 25 g of oral glucose, the AUC-60 for aGLP-1 and tGIP was significantly higher in postoperative patients. In contrast, PYY showed statistically significant higher AUC-60 for 25 g of oral glucose only (Table 2, Fig. 2). There was no statistically significant difference in fasting C-peptide or AUC-180 for C-peptide between obese and postoperative patients (Table 1, Fig. 1). Molar insulin/C-peptide ratio was significantly lower in postoperative versus obese patients (Table 1).

Lean controls versus PostOP

After LRYGB, fasting values for glucose, insulin and C-peptide as well as for HOMA and AUC-180 for insulin were not significantly different from LC (normalization). In contrast, AUC-60 for aGLP-1 was significantly higher postoperatively after both 10 g and 25 g of oral glucose (overcorrection; Table 2, Fig. 2). AUC-60 for tGIP and PYY showed statistically significant higher release in LRYGB patients compared with LC after stimulation with 25 g of oral glucose only (Table 2, Fig. 2). AUC-180 for C-peptide was significantly higher in postoperative patients compared with LC after either glucose load (Table 1, Fig. 1). No statistically significant difference was found in molar insulin/C-peptide ratio between lean versus postoperative patients (Table 1).

Gastric/pouch emptying

After 10 g and 25 g of oral glucose ingestion, gastric emptying in OC and LC was significantly slower ($P < .001$) than in postoperative patients. There was no statistically significant difference in gastric emptying rates between OC and LC. Although gastric emptying rates showed a deceleration for the higher glucose load in LC and OC (Cmax LC 10 g versus 25 g, $P = .003$; Cmax OC 10 g versus 25 g, $P = .04$), pouch emptying in postoperative patients was not significantly different after 10 g and 25 g of glucose (Fig. 3).

Discussion

The primary findings in our study are: 1) A significant increase in incretin secretion to low oral glucose loads in patients after LRYGB, and 2) a load-dependent deceleration of gastric emptying in lean and obese persons but similar pouch emptying rates in patients after LRYGB.

Table 2
Gut hormones in morbidly obese patients 6-8 weeks after LRYGB with 10 g and 25 g oral glucose stimulation

Parameter AUC-60 (pg*min/mL)	Oral load	Lean controls	Obese controls	PostOP patients	*P*-Value		
					a)	b)	c)
		|_____**a)**_____|					
		|_____**b)**_____|					
		|_____**c)**_____|					
GLP-1	10 g	908 ± 106	921 ± 115	1'808 ± 193	**<.001**	**<.001**	1.0
	25 g	1'577 ± 246	1'586 ± 239	5'015 ± 655	**<.001**	**.001**	1.0
tGIP	10 g	12'281 ± 1340	11'423 ± 835	17'170 ± 2'315	**.03**	.09	1.0
	25 g	19'945 ± 2382	18'381 ± 1531	31'259 ± 4'309	**.007**	**.02**	1.0
PYY	10 g	1'158 ± 77	1'197 ± 98	1'405 ± 165	**.61**	.4	1.0
	25 g	1'581 ± 227	1'510 ± 226	2'516 ± 271	**.03**	**.04**	1.0

AUC-60 = area under the curve 0–60 minutes; GLP-1 = glucagon-like peptide 1; LRYGB = laparoscopic Roux-ex-Y gastric bypass; PYY = peptide tyrosine tyrosine; tGIP = total glucose-dependent insulinotropic peptide.

Data are expressed as mean ± SEM, AUC (area under the curve) from 0–60 minutes. $N = 8$ PostOP, 12 obese controls and 12 lean controls.

P values: a) Obese versus PostOP, b) Lean versus PostOP, c) Lean versus Obese; (bold <.05)

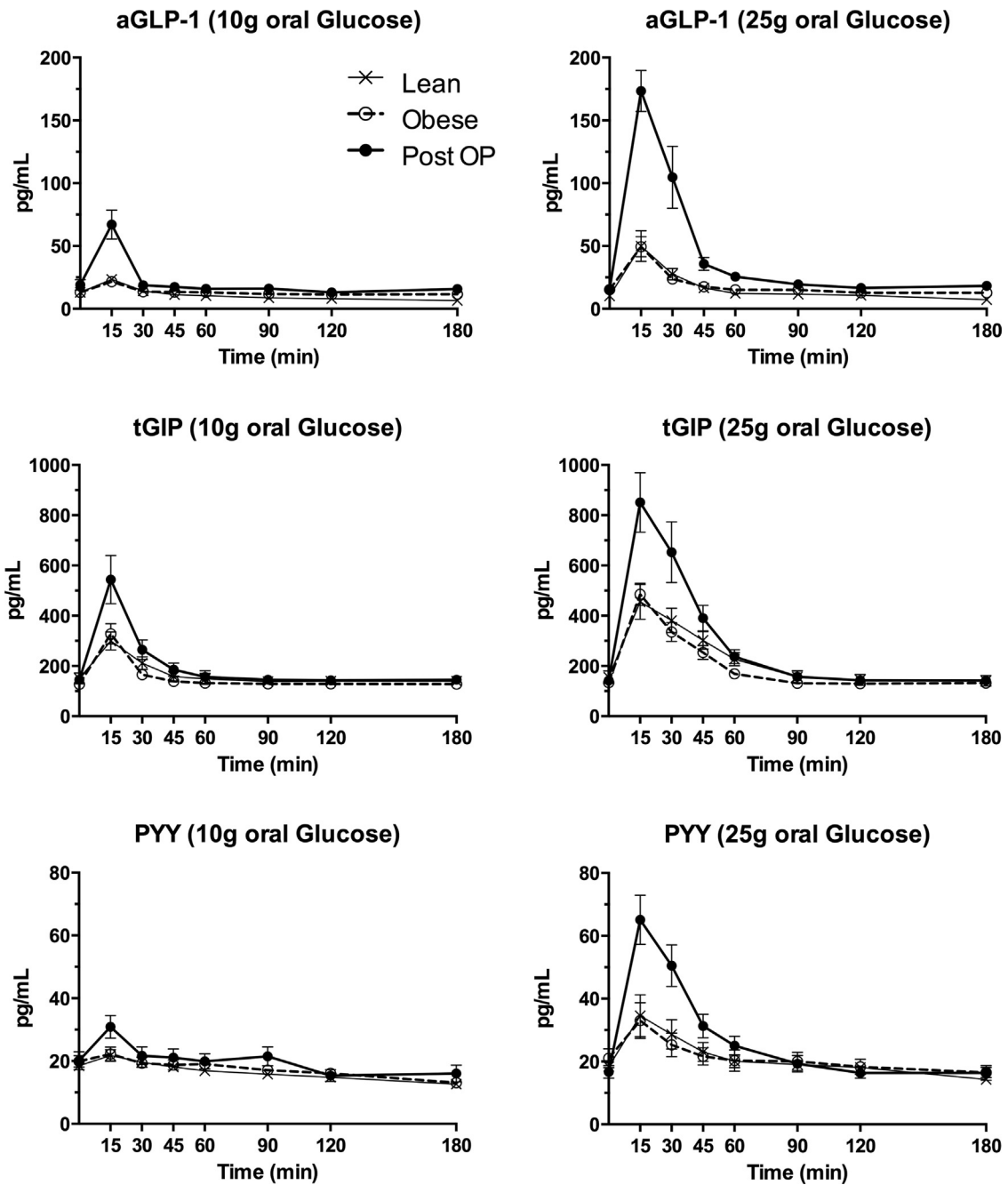

Fig. 2. Gut hormones after 10 g and 25 g glucose ingestion. Data are expressed as mean ± standard error of the mean. N = 8 PostOP (10 ± .4 weeks after laparoscopic Roux-en-Y gastric bypass), 12 obese controls, and 12 lean controls.

Symptoms of dumping syndrome after carbohydrate ingestion are quite common in patients after gastric bypass surgery. Although up to 70% of patients after LRYGB indicate symptoms of dumping syndrome if questioned, rates of severe hypoglycemia requiring hospitalization is low as demonstrated in a retrospective cohort study on 5040 cases in Sweden [6,7]. In a recent study by Roslin et al., a very high oral glucose load of 100 g was used and resulted in reactive hypoglycemia in 72% of patients [8]. However, although symptoms with medium to high doses (50–100 g) of oral glucose stimulation have been described in the literature, low dose oral glucose challenges using 10 g or 25 g are missing. Furthermore, incretin release is usually studied with medium to high doses as well. In this study, we could show that low oral glucose challenges are sufficient to characterize insulin sensitivity and to stimulate incretin release; a 25 g load of oral glucose results in reliable secretion of incretin hormones not only after bypass surgery but also in lean and obese controls. Increased release of GLP-1, GIP, and PYY after gastric bypass

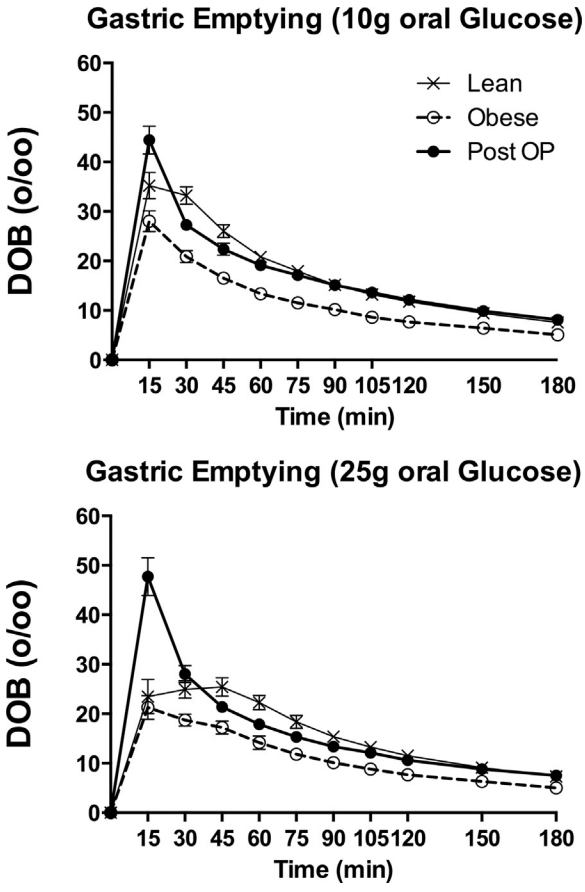

Fig. 3. Gastric emptying respectively pouch emptying after 10 g and 25 g glucose ingestion. DOB = δ over basal. Data are expressed as mean ± standard error of the mean. N = 8 PostOP (10 ± .4 weeks after laparoscopic Roux-en-Y gastric bypass), 12 obese controls, and 12 lean controls.

surgery compared with obese non-operated patients (as previously documented in several other studies [9]) could also be demonstrated here with 25 g of glucose. We did not include a higher load of glucose in the trial to avoid unwanted effects in the postoperative setting; this can be interpreted as a limiting factor.

Aside from the option to use 25 g of glucose in clinical trials with bariatric patients, circumventing the problem of adverse events such as dumping syndrome while still sufficiently stimulating insulin and incretin release, a possible clinical implication might lie in the potential to use 25 g as an oral glucose tolerance test in patients after LRYGB, for instance during pregnancy. For this purpose, obviously, larger study populations are needed, and the 25 g OGTT would have to be validated against conventional strategies to diagnose glucose intolerance.

A progressive, dose-dependent rise in plasma insulin and C-peptide occurred (assessed by AUCs and peak concentrations) in response to both glucose loads, both in lean and obese patients. The increase in plasma insulin was significantly higher in the obese group, confirming that obese patients have an impaired glucose homeostasis and exhibit prediabetic factors, including hyperinsulinemia and insulin resistance. To investigate whether insulin secretion is altered in obese persons, we also measured C-peptide levels. Hepatic extraction of C-peptide is negligible, although the liver is a major site of insulin extraction (first-pass effect); changes in the molar ratio would therefore reflect changes in hepatic insulin extraction. The observed differences between fasting insulin and C-peptide concentrations in obese persons would therefore suggest that the molar ratio is altered; we infer from these observations that insulin disposal is changed in obese persons.

Gastric emptying was measured by means of a breath test with ^{13}C-sodium acetate. We found that gastric emptying after oral glucose intake is similar in obese compared with lean controls. In the literature, differences in gastric emptying rates between obese and lean humans are still controversially discussed. Some groups reported gastric emptying to be similar to, faster, or slower in obese compared with lean humans. There are several reasons for these discrepancies: For example, methodologies used to assess gastric emptying and differences in meal composition (e.g., fat content) and consistency (liquid versus solid) [10–13].

As for postoperative patients, with their altered anatomy, it is challenging to interpret differences seen between these patients and the control groups. The applied method is an indirect way of measuring gastric emptying (depending on ^{13}C absorption, metabolization in the liver, and appearance of $^{13}CO_2$ in the exhaled air). Rather than speaking of gastric emptying, we can summarize that in the obese and lean controls, it takes longer for the ingested ^{13}C to appear as $^{13}CO_2$ in breath samples compared with postoperative patients. In addition, we could observe that although gastric emptying can vary in non-operated patients depending on the amount of glucose ingested with a deceleration in the higher load, patients after gastric bypass no longer have such an option because of the exclusion of the pylorus, resulting in a functionally rigid tube; independently of the glucose load, $^{13}CO_2$ appears in the breath sample with the same speed.

Limitations of the study include the following: In the postoperative group, only females were included, whereas the control groups included both sexes (50/50%). Larger sample sizes and inclusion of both genders might be worthwhile in future studies.

Conclusion

We conclude that 25 g of oral glucose leads to reliable stimulation of gut hormones in lean and obese patients as well as postoperative patients and does not provoke dumping syndrome.

Disclosures

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Editorial comment

"Metabolic preparation" before metabolic surgery

With rising volumes of gastric bypass procedures for morbid obesity, the number of patients presenting with symptoms of early and/or late dumping is increasing. The mechanisms are generally believed to be associated with a faster delivery of nutrients, in particular carbohydrates, to distal parts of the gut with altered release of gastrointestinal hormones after oral intake. Somewhat surprising, dumping and hypoglycemia is reported also after sleeve gastrectomy [1], suggesting that other mechanisms might be involved as well.

Besides continuous glucose monitoring, hormonal and metabolic response to an oral challenge is one of the most important diagnostic tools for evaluation of patients with suspected dumping or hypoglycemia after bariatric surgery. A regular oral glucose tolerance test containing 75 g glucose may, however, induce severe symptoms by itself after gastric bypass. In the current issue of *SOARD*, Wölnerhanssen et al. [2] evaluate hormonal response and gastric emptying rate in lean, obese, and postgastric bypass surgery patients in response to 2 lower doses of glucose (10 and 25 g, respectively). They report that the higher of these doses (25 g) induces a "relevant" incretin response without significant symptoms of dumping or hypoglycemia and conclude that this amount could be safely and accurately used for evaluation of patients after gastric bypass.

Furthermore, they report that obese patients display slower gastric emptying rates than lean individuals and that this difference does not persist after laparoscopic gastric bypass (LRYGB). The rate of gastric emptying in obese individuals may have implications also for other aspects of metabolic alterations after surgery. Although bariatric surgery improves insulin sensitivity and glucose control, in particular in patients with type 2 diabetes, surgical trauma by itself induces a state of insulin resistance in the immediate postoperative period [3]. By avoiding preoperative fasting using a carbohydrate-rich drink (CHO), the degree of postoperative insulin resistance has been shown to be reduced by approximately 50% [4], which in turn is associated with improved postoperative recovery [5]. Therefore, the use of preoperative CHO is recommended in most Enhanced Recovery After Surgery (ERAS) guidelines for major abdominal surgery. Whether preoperative CHO should be recommended for patients undergoing bariatric